Influence of sociocultural factors on the ovulatory status of polycystic ovary syndrome

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Objective: To evaluate the role of social and cultural differences inside the same ethnic group on the ovulatory status of women with polycystic ovary syndrome (PCOS).
Design: To correlate social and cultural status with the phenotypic expression (body weight and ovulation) and with androgen and insulin levels of PCOS.
Setting: University department of medicine.
Patient(s): Two hundred and forty-four consecutive PCOS women.
Intervention(s): All studied patients completed a simple questionnaire to indicate their mean family income and their school education.
Main Outcome Measure(s): Ovulation was assessed by measurement of serum progesterone on day 22 of a spontaneous or induced menstrual cycle. Levels of blood testosterone, sex hormone–binding globulin, insulin, and blood glucose were evaluated.
Result(s): In the low to medium income group, 21% of patients had ovulatory PCOS, but the prevalence of the same PCOS phenotype was 43% in patients with high income. In patients with low education, only 12% presented with ovulatory PCOS compared with 47% of the patients with high education status. Mean family income negatively correlated with body mass index, waist circumference, insulin, and insulin resistance. Serum progesterone correlated negatively with insulin and insulin resistance.
Conclusion(s): In an ethnically homogeneous PCOS population, high socioeconomic status was associated with a higher prevalence of the ovulatory phenotype. Differences in ovulatory status between the social classes seem to be related to differences in insulin levels and fat quantity and distribution. (Fertil Steril® 2009;91:1853–6. ©2009 by American Society for Reproductive Medicine.)
Key Words: PCOS, social class, insulin, obesity

Polycystic ovary syndrome (PCOS) is a heterogeneous disorder that may present with very different clinical patterns (1–3). Many of these differences are probably related to differences in genetic expression of androgen excess and/or insulin resistance, but some may depend on environmental influences on body weight and fat distribution (1, 4). In particular, increased abdominal fat mass worsens hyperandrogenism and insulin resistance and may modify the ovulatory status of some women with PCOS, moving the patients from mild ovulatory forms to the severe anovulatory disorder (1, 4). In addition, in many women with the anovulatory form of PCOS, reduction of body weight by diet is sufficient to induce ovulation and bring back the patient to the ovulatory form (5).

In the past, most studies evaluating the effect of body weight on PCOS phenotype have focused on differences among different populations (2, 6, 7). In fact, in some countries such as the United States, most patients with PCOS are obese; in other countries, such as southern Italy or Japan, the mean body weight of PCOS patients is lower. Accordingly, the milder ovulatory forms of PCOS seem more common in southern Italy than in the United States, confirming that the mean body weight of a population may influence the prevalence of infertility disturbances inside that population (8, 9).

Social differences inside the same ethnic group also may be important in determining body weight. In fact, in poor societies, body weight is higher in people with higher socioeconomic status (10). The opposite is found in affluent societies, where increased body weight is more commonly found among those in lower socioeconomic classes (11–14). Recent studies have shown that in the United States obesity is more common in those with lower income (12, 13); in Singapore, not only income but also education strongly influenced the mean body weight (14).

Our study examined an ethnically homogeneous population of women with PCOS to evaluate the influence of several sociocultural factors (family income and education) on ovulatory status as well as several clinical (body weight and fat distribution) and endocrine (androgen and insulin levels) factors.

MATERIALS AND METHODS

Our study enrolled 244 women with PCOS who had been consecutively referred to the Endocrine Unit of the Department of Clinical Medicine of the University of Palermo for symptoms of hyperandrogenism. The diagnosis of PCOS was based on findings of polycystic ovaries and/or chronic anovulation (15, 16). The presence of polycystic ovaries was determined by intravaginal sonography, in which increased ovarian size and/or of at least 12 follicular cysts measuring 2 to 9 mm were considered indicative (17, 18).

No patients with adrenal enzymatic deficiencies, hyperprolactinemia, Cushing syndrome, or androgen secreting tumors were included in this study. Normal circulating levels of 17-hydroxyprogesterone (<3 $\mu g/L$) were used to exclude the diagnosis of nonclassic 21-hydroxylase deficiency (19). Clinical data and/or urinary cortisol (<60 $\mu g/day$) assessment were used to exclude the diagnosis of Cushing syndrome (20), and normal levels of prolactin (<25 ng/mL) used to exclude hyperprolactinemia (9). Patients with androgen secreting tumors were excluded through very high androgen levels (total testosterone >150 ng/dL or serum DHEAS >8000 $\mu g/L$), and tumors were demonstrated by computed tomography or magnetic resonance imaging (9).

In all patients, body mass index (BMI) and waist circumference were determined. All of the women were sedentary and were not participating in any specific diet plans at the time of the study.

During the follicular phase (days 5 to 8) of a spontaneous or progestin-induced cycle, levels of serum testosterone (T), sex hormone–binding-globulin (SHBG), insulin, and blood glucose were measured. Serum progesterone was measured on days 21 to 24 of a spontaneous or induced menstrual cycle. Anovulation was defined as serum progesterone <3 ng/mL. In patients with normal menses, at least two consecutive low levels of serum progesterone (<3 ng/mL) were needed to make a diagnosis of anovulation. Serum hormone levels were quantified by well-established methods that have been validated previously in our laboratory (3). Serum testosterone was measured by specific radioimmunoassays after extraction, using methods previously described elsewhere (3). Serum progesterone, SHBG, and insulin were measured by commercial radioimmunoassay methods. Insulin resistance was calculated by the Quantitative Insulin-Sensitivity Check Index (QUICKI) (21). Blood glucose was determined using the glucose oxidase method. In all assays, intra-assay and interassay coefficients of variation did not exceed 6% and 15%, respectively.

All studied patients completed a simple questionnaire to indicate their family income and their school education.

Because in Sicily, according to the Italian Government Statistical Office (22), mean family income is 19,380 euros/year, the patients were asked to define their family income in one of these three categories: $<15,000$ euros/year, between 15,000 and 30,000 euros/year, or $>30,000$ euros/year to represent low family income, medium family income, and high family income, respectively.

The patients also were asked to provide their highest education level. Because education is compulsory in Italy until middle school, patients whose highest education level was primary or middle school were considered to have a low education level, and patients who had completed high school or university were considered to have a high education status.

Institutional review board approval was obtained, and all patients and controls gave written consent.

Statistical Analyses

Analysis of covariance was used for comparisons. Post hoc testing was carried out by Student's t-test with log transformation. Pearson product moment correlation and stepwise multivariate linear regression analysis with forward selection were used to analyze correlations. $P<.05$ was considered statistically significant. All data are expressed as mean $\pm$ standard deviation.

RESULTS

The PCOS patients in the study had a mean age of 25 ± 5 years, a mean BMI of 28 ± 5, and a mean waist circumference of 91 ± 10 cm. Among the patients, 164 (67%) were anovulatory (classic PCOS) and 80 (33%) were ovulatory (ovulatory PCOS). The anovulatory PCOS patients (classic PCOS) had similar age but higher BMI (28.9 ± 5 vs. 26 ± 5, $P<.01$) and larger waist circumference (93 ± 14 vs. 87 ± 9 cm, $P<.01$) than the ovulatory PCOS patients. The levels of serum testosterone, SHBG, and insulin were statistically significantly ($P<.01$) higher and insulin sensitivity was statistically significantly ($P<.01$) lower in patients with classic PCOS than in patients with ovulatory PCOS.

In terms of income, 130 patients had a high family income whereas 51 had a low family income and 63 a medium family income. The patients with low or medium family income did not differ in terms of body weight, waist circumference, ovulatory status, or endocrine parameters (Table 1), but both groups had statistically significantly higher values for anovulation, mean BMI, mean waist, and mean insulin level and lower QUICKI scores than the patients with high family income (see Table 1). In total, 78.9% of patients with low-medium family income had classic PCOS (and the remaining 21.1% presented with ovulatory PCOS); the prevalence of classic PCOS in patients with high income was 57% (and 43% of patients had ovulatory PCOS) (Fig. 1).

In terms of education, 104 patients had a low education, and 140 patients had a high education status. Patients with low education had a statistically significantly higher prevalence of anovulation and statistically significantly higher values for BMI, waist circumference, insulin levels and a lower QUICKI score than the patients with high education status (see Table 1). Among the patients with low education, 88% had classic PCOS and only 12% had ovulatory PCOS; among patients of higher sociocultural status, classic PCOS was found in 53% and ovulatory PCOS in 47% (Fig. 2).

There was a good correlation between family income and educational status ($r = 0.68$, *P*<.01). However, a minority of patients (27 women, 11%) were low or medium income with a high education status or vice versa (12 women, 5%). In these patients, educational status seemed more important than income in determining ovulatory status: anovulation was present in 70% of patients with low to medium family income but high educational status, and in 88% of patients with high family income but low educational status.

Mean family income negatively correlated with BMI (r = −0.42, *P*<.01); a higher correlation was with waist circumference ($r = -0.70$, *P*<.01). Income negatively correlated with serum insulin ($r = -0.41$, *P*<.01) and positively with SHBG ($r = 0.47$, *P*<.01) and with QUICKI ($r = 0.45$, *P*<.01) but not with serum testosterone or progesterone. Independent of the socioeconomic components, serum progesterone correlated positively with serum SHBG ($r = 0.29$, *P*<.01), with insulin (r = 0.29, *P*<.01), and with insulin sensitivity (with QUICKI: $r = 0.28$, *P*<.01) but not with BMI, waist, or serum testosterone.

DISCUSSION

Our data show that, in an ethnically homogeneous population of women with PCOS, low socioeconomic status is associated with a higher prevalence of the anovulatory phenotype (classic PCOS). Only 12% to 20% of the patients of lower socioeconomic status had the ovulatory phenotype whereas ovulation was found in almost 50% of the patients with high income and/or education.

The mechanisms that determine anovulation in PCOS are imperfectly understood. In fact, mild/moderate androgen excess alone is not sufficient to induce chronic anovulation (e.g., in many patients with nonclassic 21-hydroxylase deficiency or in patients with idiopathic hyperandrogenism) (9). Similarly, although simple obesity is associated with insulin resistance, often it presents with normal ovulatory
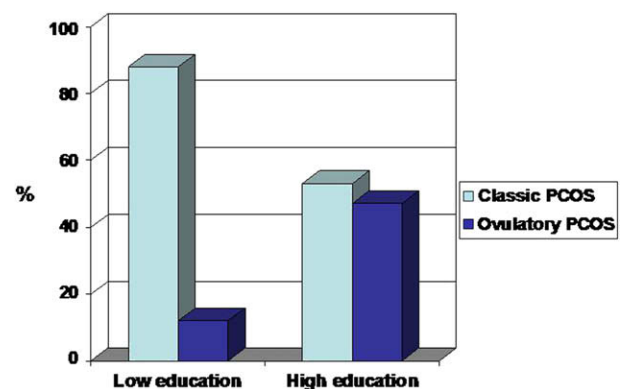
FIGURE 1

Influence of mean family income on ovulation in 244 women with polycystic ovary syndrome.
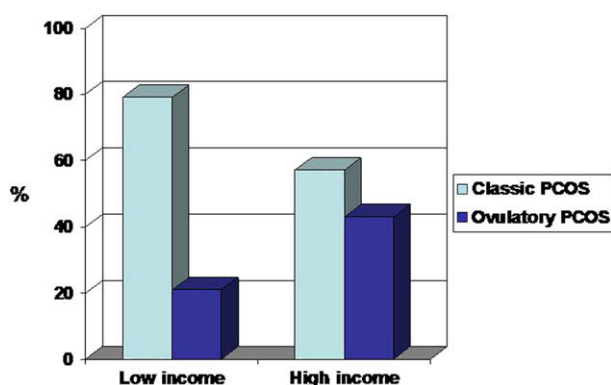
Di Fede. Social classes and ovulation in PCOS. Fertil Steril 2009.

FIGURE 2

Influence of education on ovulation in 244 women with polycystic ovary syndrome.

Di Fede. Social classes and ovulation in PCOS. Fertil Steril 2009.

menstrual cycles. It is probable that, in many women, both androgen excess and hyperinsulinemia are needed to determine anovulation, and in hyperandrogenic patients an increase of circulating insulin may be the main determinant of chronic anovulation (1).

Our data confirm a statistically significant negative correlation between serum insulin (and insulin resistance) and values of circulating progesterone in hyperandrogenic PCOS patients. We found no correlation for serum testosterone with circulating progesterone.

In this study, patients with low/medium family income and/or low education presented with higher BMI, increased waist circumference, higher insulin levels, and more severe insulin resistance than the patients with high family income and/or high education. It is probable that the greater prevalence of anovulation in patients with low/medium family income and/or low education was a consequence of differences in fat quantity and distribution and in insulin sensitivity. This suggests that, in women with PCOS, socioeconomic status does influence ovulation because of its effects on insulin secretion and sensitivity, which are a consequence of increased body weight but mostly of increased abdominal fat quantity. In fact, women of low socioeconomic status (mean family income) presented with the highest correlation with waist circumference, a sensitive indicator of abdominal obesity.

Generally, family income and education were well correlated; however, in the patients presenting with low family income and high education or vice versa, education seemed more important than income in determining their ovulatory status. Thus, at least in a subgroup of patients with PCOS, anovulation seems to be secondary to abdominal obesity, which may be determined by environmental influences including low socioeconomic status. It is probable that PCOS patients with lower family income but mainly of low education are less informed or less sensitive to the importance of their lifestyle and thus develop abdominal obesity with higher frequency.

Our findings on the effects of socioeconomic status in PCOS are new, but they are not surprising and probably represent only an extension of a phenomenon that effects the general population. Several studies have demonstrated that, in affluent societies, increased body weight is more commonly found in those of lower socioeconomic classes (11–14).

Sociocultural factors, which influence body weight, fat distribution, and insulin circulating levels, are very important in the ovulatory status of PCOS patients. We need to take stronger measures to educate women of lower socioeconomic classes to the importance of their lifestyles, which may improve not only their cardiovascular and metabolic risks but also reduce problems of infertility and the related costs.

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